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(71) Applicant: Talcher, Zvi  
25 Ben Yehuda Street  
Rehovot(IL)

(72) Inventor: Talcher, Zvi  
25 Ben Yehuda Street  
Rehovot(IL)  
Inventor: Shporer, Mordechai  
14 Shachar Street  
Rehovot(IL)

(74) Representative: JENSEN & SON  
8 Fulwood Place High Holborn  
London WC1V 6HG(GB)

(54) Remote temperature control monitoring apparatus and technique.

(57) A thermometry system comprising an implantable element having temperature dependent NMR properties, apparatus for applying an RF field to the implantable element, and apparatus for sensing the temperature dependent NMR response of the implantable element and for providing an output indication of temperature of the implantable element.

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## REMOTE TEMPERATURE MONITORING APPARATUS AND TECHNIQUE

### FIELD OF THE INVENTION

The present invention relates to temperature monitoring apparatus and techniques using magnetic resonance generally.

### BACKGROUND OF THE INVENTION

Temperature monitoring apparatus and techniques using magnetic resonance are known in the art.

Temperature measurements based on Nuclear Quadrupole Resonance (NQR) are described in the following references:

Yu. N. Bubkov, R. Sh. Lotfullin, R.V. Majera, and A.A. Buguslavskii - "Pulsed NQR thermometer for temperatures up to 870 degrees K", *Izvestiya Akademii Nauk SSSR, Seriya F.Z. Chesкая*, Vol. 39, No. 12, 1975, pp. 2655 - 2660;

D.B. Utton, J. Vanier - "Thermometry by Nuclear Quadrupole Resonance", *Instrumentation Technology*, December 1976, pp. 47 - 52;

A. Ohte and H. Iwaka - "A new nuclear quadrupole resonance standard thermometer" *Temperature*, American Institute of Physics, 1982, pp 1173 - 1180.

The essential feature of the NQR technique is measurement of temperature-dependent NQR frequencies which are an intrinsic property of the material used to construct an NQR sensor.

In laboratory contexts wherein various types of magnetic resonance were used to measure parameters of material structure, such as the lattice magnetic field, the temperature dependence of nuclear magnetic resonance (NMR) frequencies has been investigated. Reference is made in this context to S. Ogawa and S. Morimoto, - "Nuclear Magnetic Resonance of Fe<sup>57</sup> in Various Ferromagnetic Oxides", *Journal of the Physical Society of Japan*, Vol. 17, No. 4, April, 1962, pp 654 - 659.

Thermometry systems in conventional use in clinical hyperthermia include probes employing thermocouples and thermistors having non-metallic output leads, so as not to interfere with the applied electromagnetic fields. Where multiple location temperature sensing is required, this is conventionally accomplished by moving the probe from location to location or by employing a plurality of such probes.

The state of the art in the use of thermometry systems in clinical hyperthermia is described in G.M. Samaras, A.Y. Cheung, "Microwave hyper-

thermia for cancer therapy", *CRC Critical Reviews in Bioengineering*, February, 1981, pp. 123 - 184. Some of the techniques described in the foregoing article are based on temperature dependence of optical parameters of given substances, such as GaAs, and liquid crystals. The advantages of such techniques are that output communication is provided by optical fiber leads, which do not interfere with the applied electromagnetic field. A multiple GaAs sensor is described in V.A. Vaguine, D. A. Christensen, J.H. Lindley, T.E. Walston, "Multiple sensor optical thermometry system for application in clinical hyperthermia", *IEEE Transactions on Biomedical Engineering*, Vol. BME-31, No. 1, January, 1984, pp 168 - 172.

The use of conventional thermometry systems in clinical hyperthermia provides relatively poor reproducibility over time and relatively poor spatial resolution, in view of the fact that the probes are inserted prior to each treatment. The use of conventional probes naturally involves very significant patient discomfort and is time intensive and costly.

A number of proposed methods of noninvasive thermometry are described in T. C. Cetas, "Will thermometric tomography become practical for hyperthermia treatment monitoring?", *Cancer Research (SUPPL.)* 44, October, 1984, 4805s - 4808s. The methods proposed therein all involve unsatisfactory compromises between reading rate, temperature sensitivity, spatial discrimination, stability and reproducibility.

It has been proposed to employ non-zero external static magnetic field NMR for directly measuring the temperature of living tissue in vivo in a clinical hyperthermia context. Such proposals are based on temperature dependence of NMR relaxation times and are described in the following publications:

D.L. Parker, "Application of NMR imaging in hyperthermia: an evaluation of the potential for localized tissue heating and noninvasive temperature monitoring", *IEEE Transactions on Biomedical Engineering*, Vol. BME-31, No. 1, January, 1984, pp 161 - 167; and

S. Petersson, J. Saaf, M. Bolmsjo, B. Persson, "Temperature mapping using an Ultra Lowfield MR scanner", *Sixth Annual Meeting of Society of Magnetic Resonance in Medicine*, August 17 - 21, 1987, New York City, U.S.A.

If realized, the technique described in the preceding two publications would provide non-invasive direct measurement of temperature of living tissue. However, it would require expensive instrumentation which would have to be compatible with clinical hyperthermia apparatus. Moreover, the relax-

ation parameters are not uniform in different subjects. Therefore, in order to establish an absolute temperature output, a complicated calibration procedure would be required.

### SUMMARY OF THE INVENTION

The present invention seeks to provide a relatively low cost, easy to use, wireless thermometry system which is useful, *inter alia*, in clinical hyperthermia.

There is thus provided in accordance with a preferred embodiment of the present invention a thermometry system comprising an implantable element having temperature dependent NMR properties, apparatus for applying an RF (radio frequency) electromagnetic field to the implantable element, and apparatus for sensing the temperature dependent NMR response of the implantable element and for providing an output indication of temperature of the implantable element.

There is also provided in accordance with a preferred embodiment of the present invention a technique for *in vivo* temperature measurement of tissue comprising the steps of:  
implanting in living tissue an element having temperature dependent NMR properties,  
applying an RF field to the element;  
sensing the temperature dependent NMR response of the element; and  
providing an output indication of temperature of the implantable element.

There is also provided in accordance with a preferred embodiment of the present invention a clinical hyperthermia system comprising apparatus for selectably heating tissue *in vivo*, apparatus for monitoring the temperature of the tissue including at least one implantable element having temperature dependent NMR properties, apparatus for applying an RF field to the implantable element, and apparatus for sensing the temperature dependent NMR response of the implantable element and for providing an output indication of temperature of the implantable element.

There is also provided in accordance with a preferred embodiment of the present invention a technique for localized heating of living tissue comprising the steps of:  
implanting in living tissue at least one element having temperature dependent NMR properties,  
selectably heating living tissue;  
applying an RF field to the element;  
sensing the temperature dependent NMR response of the element; and  
providing an output indication of temperature of the implantable element.

In accordance with an embodiment of the present invention, the implanted element may remain in the tissue over an extended period, such as weeks and months, over which multiple clinical hyperthermia treatments may occur.

Additionally the implanted element does not require calibration.

Further in accordance with an embodiment of the invention, where a plurality of implanted elements are employed, they may be constructed to have different nuclear magnetic resonance frequency ranges so as to enable simultaneous measurement of temperatures at multiple locations.

Additionally in accordance with a preferred embodiment of the invention, the step of selectably heating tissue *in vivo* comprises the step of applying an RF heating field thereto and the technique also comprises measuring the distribution of the RF heating field at an NMR resonance frequency of said at least one element.

In accordance with the foregoing embodiment of the invention, the apparatus for applying an RF field forms part of the apparatus for selectably heating tissue and the step of measuring the distribution of the RF heating field takes place at times other than those at which an RF heating field is applied in a time shared arrangement and at a different frequency than that of the RF heating field.

### BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated from the following detailed description, taken in conjunction with the drawings in which:

Fig. 1 is a block diagram illustration of a thermometry system constructed and operative in accordance with a preferred embodiment of the present invention; and

Fig. 2 is a block diagram illustration of clinical hyperthermia apparatus constructed and operative in accordance with a preferred embodiment of the invention.

### DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

Reference is now made to Fig. 1, which illustrates a thermometry system constructed and operative in accordance with a preferred embodiment of the present invention. One or more implantable passive elements 10 having magnetic resonance properties, such as resonance frequency and NMR

signal amplitude which have a known temperature dependency, are implanted in vivo in a living organism, such as the human body. The passive elements 10, which will be described hereinafter in greater detail, may be located in or near a tumor 12 or other body which is sought to be heated in a precisely controlled manner.

An RF transmitter 20, including a power amplifier such as a Model 200L manufactured by Amplifier Research of Souderton, Pa. 18984, U.S.A., provides an RF output via an antenna 21 and a matching network 22. The RF transmitter 20 receives a signal input from an RF driver 24, such as a Model 410, manufactured by Matec Instruments, Inc. of 60 Montebello Road, of Warwick, RI 02886, U.S.A., modified to operate at higher frequencies, which also receives inputs from a pulse programmer 26. Pulse programmer 26 includes a number of triggers, the timing of which is controlled by a computer 30, such as an IBM PC. The pulse programmer 26 and the RF driver 24 both receive a clocking input from a frequency source 28, such as a Model 5120A, manufactured by Wavetek San Diego Inc. of 9045 Balboa Ave. San Diego, California 92122, U.S.A..

A preamplifier 32, such as a Model 254 manufactured by Matec, receives, via antenna 21 and matching network 22 magnetic resonance signals from elements 10, which contain temperature information. The preamplifier 32 provides an output to a receiver 34, such as a Model 615 manufactured by Matec, which also receives RF signal phase information from driver 24.

The receiver 34 provides an output to a transient recorder 36, such as a Gould Model 4035 which also receives timing information from pulse programmer 26. The output of transient recorder 36 is supplied to computer 30, which provides an output indication of the temperature at elements 10.

Elements 10 each include material such as iron garnet having the following chemical composition:  $5\text{Fe}_2\text{O}_3\text{M}_2\text{O}_3$ , wherein M is a rare earth metal. The internal magnetic field which determines the resonance frequency can be controlled by using an appropriate rare earth metal. For example, if M is Yttrium, the resonance frequency of element 10 at about 30 degrees C is approximately 53.578 MHz. The temperature dependence is about 60 KHz/degree C when the resonance frequency can be determined with accuracy of about 1 KHz. This leads to temperature resolution which is much better than 0.1 degree C, which is ordinarily required for clinical hyperthermia.

Reference is now made to Fig. 2, which illustrates the thermometry system of the present invention in the context of a clinical hyperthermia system. A conventional clinical hyperthermia sys-

tem such as model BSD-2000 manufactured by BSD Medical Corporation of 420 Chipeta Way, Salt Lake City, Utah 84108 USA, incorporates a control and safety monitoring unit 40, having an associated operator panel 42 and display 44.

Unit 40 operates a RF power generator 46, which alternatively could be a microwave power generator, which drives an applicator 48 via a tuning and matching network 50. The thermometry system of the present invention interfaces with the control and safety monitoring unit 40 and computer 30 (Fig. 1) or part thereof may be incorporated in unit 40. With the exception of all or part of computer 30 and the antenna and matching networks 21 and 22, the remainder of the system of Fig. 1 is shown as being incorporated in a temperature monitor 52.

Additionally in accordance with a preferred embodiment of the invention, the step of selectably heating tissue in vivo comprises the step of applying an RF heating field thereto and the technique also comprises measuring the distribution of the RF heating field at an NMR resonance frequency of said at least one element.

In accordance with the foregoing embodiment of the invention, the apparatus for applying an RF field forms part of the apparatus for selectably heating tissue, i.e. the same antenna may be used as the transceiver antenna 21 and the applicator 48, and the step of measuring the distribution of the RF heating field takes place at times other than those at which an RF heating field is applied in a time shared arrangement and at a different frequency than that of the RF heating field.

It will be appreciated by persons skilled in the art that the present invention is not limited by what has been particularly shown and described hereinabove. Rather the scope of the present invention is defined only by the claims which follow:

## Claims

1. A thermometry system comprising:  
at least one implantable element having temperature dependent NMR properties;  
means for applying an RF field to the at least one implantable element, and apparatus for sensing the temperature dependent NMR response thereof and for providing an output indication of temperature thereof.

2. A thermometry system according to claim 1 and wherein said at least one implantable element comprises iron garnet having the following chemical composition:  $5\text{Fe}_2\text{O}_3\text{M}_2\text{O}_3$ , wherein M is a rare earth metal.

3. A thermometry system according to claim 1 and wherein said means for applying an RF field comprises a matching network and an RF antenna.

4. A thermometry system according to claim 1 and wherein said at least one implantable element does not require calibration.

5. A thermometry system according to claim 1 and wherein said at least one implantable element comprises a plurality of implanted elements, each having different nuclear magnetic resonance frequency ranges so as to enable simultaneous measurement of temperatures at multiple locations.

6. A technique for in vivo temperature measurement of tissue comprising the steps of: implanting in living tissue at least one element having temperature dependent NMR properties; applying an RF field to the at least one element; sensing the temperature dependent NMR response of the at least one element; and providing an output indication of temperature of the at least one element.

7. A technique according to claim 6 and wherein said element remains implanted in the tissue over an extended period, such as weeks and months, over which multiple clinical hyperthermia treatments may occur.

8. A clinical hyperthermia system comprising: means for selectably heating tissue in vivo; and means for monitoring the temperature of the tissue including: . at least one implantable element having temperature dependent NMR properties; means for applying an RF field to the implantable element; and means for sensing the temperature dependent NMR response of the implantable element and for providing an output indication of temperature of the implantable element.

9. A system according to claim 8 and wherein said at least one implantable element comprises iron garnet having the following chemical composition:  $5\text{Fe}_2\text{O}_3\cdot 3\text{M}_2\text{O}_3$ , wherein M is a rare earth metal.

10. A system according to claim 8 and wherein said means for applying an RF field comprises a matching network and an RF antenna.

11. A system according to claim 8 and wherein said RF antenna is also employed as part of said means for selectably heating.

12. A system according to claim 8 wherein said means for selectably heating tissue in vivo comprises means for applying an RF heating field thereto and wherein said system also comprises means for monitoring the field distribution of said RF heating field.

13. A technique for localized heating of living tissue comprising the steps of: implanting in living tissue at least one element

having temperature dependent NMR properties, selectably heating living tissue; applying an RF field to the at least one element; sensing the temperature dependent NMR response of the element; and providing an output indication of temperature of the implantable element.

14. A technique according to claim 13 and wherein said at least one implanted element may remain in the tissue over an extended period, such as weeks and months, over which multiple clinical hyperthermia treatments may occur.

15. A technique according to claim 13 and wherein said at least one implanted element does not require calibration.

16. A technique according to claim 13 and wherein in said implanting and sensing steps a plurality of implanted elements are employed, each having different nuclear magnetic resonance frequency ranges so as to provide simultaneous measurement of temperatures at multiple locations.

17. A technique according to claim 13 and also comprising the step of sensing an electromagnetic field applied for heating the tissue.

18. A technique according to claim 13 and wherein the step of selectably heating tissue in vivo comprises the step of applying an RF heating field thereto and the technique also comprises measuring the distribution of the RF heating field at an NMR resonance frequency of said at least one element.

19. A technique according to claim 18 and wherein said step of measuring the distribution of the RF heating field takes place at times other than those at which an RF heating field is applied in a time shared arrangement and at a different frequency than that of the RF heating field.

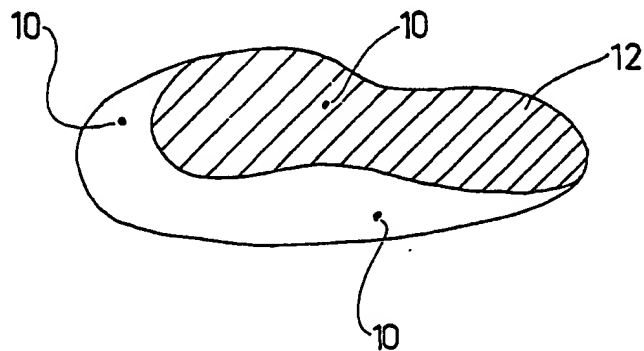
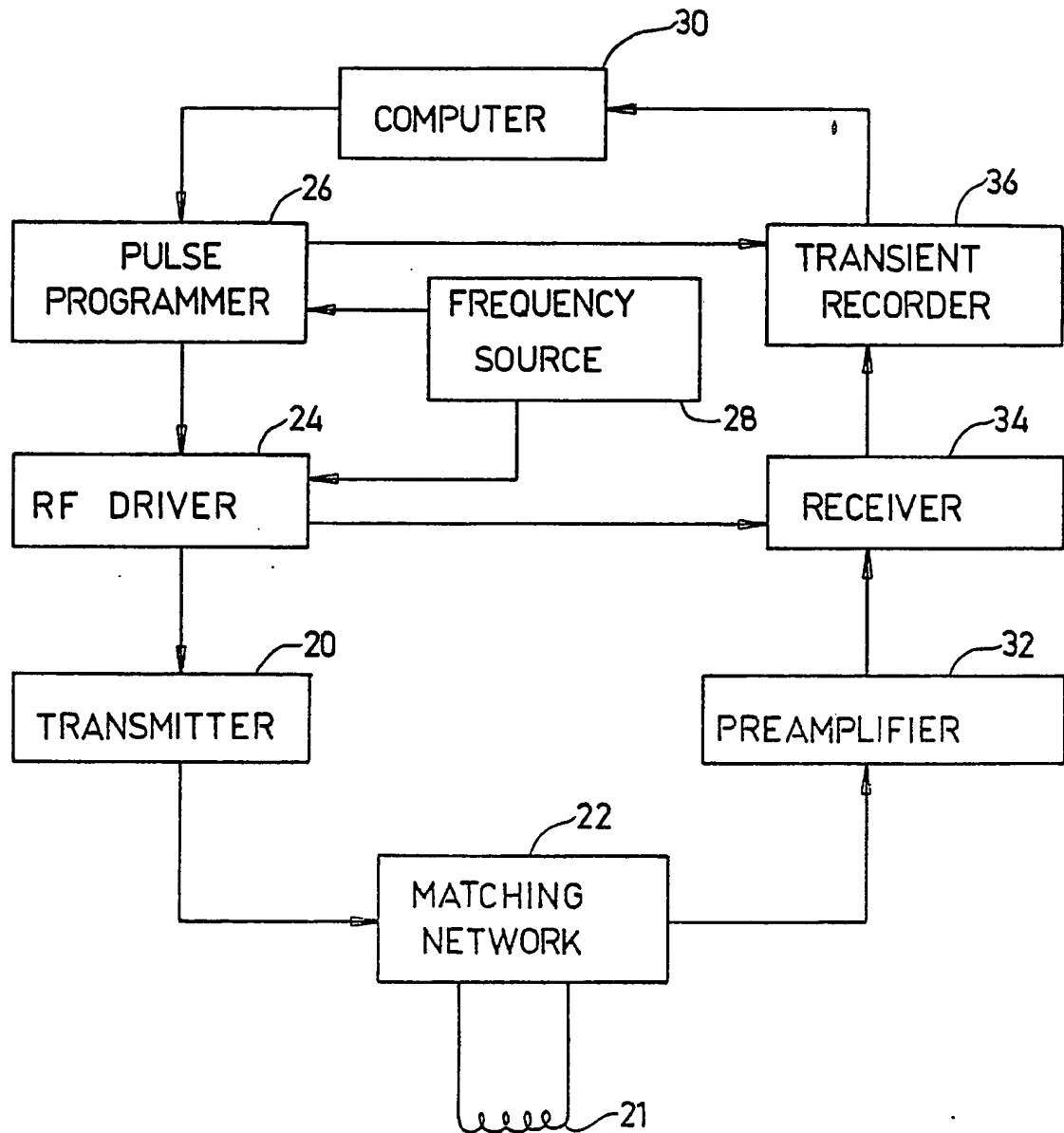
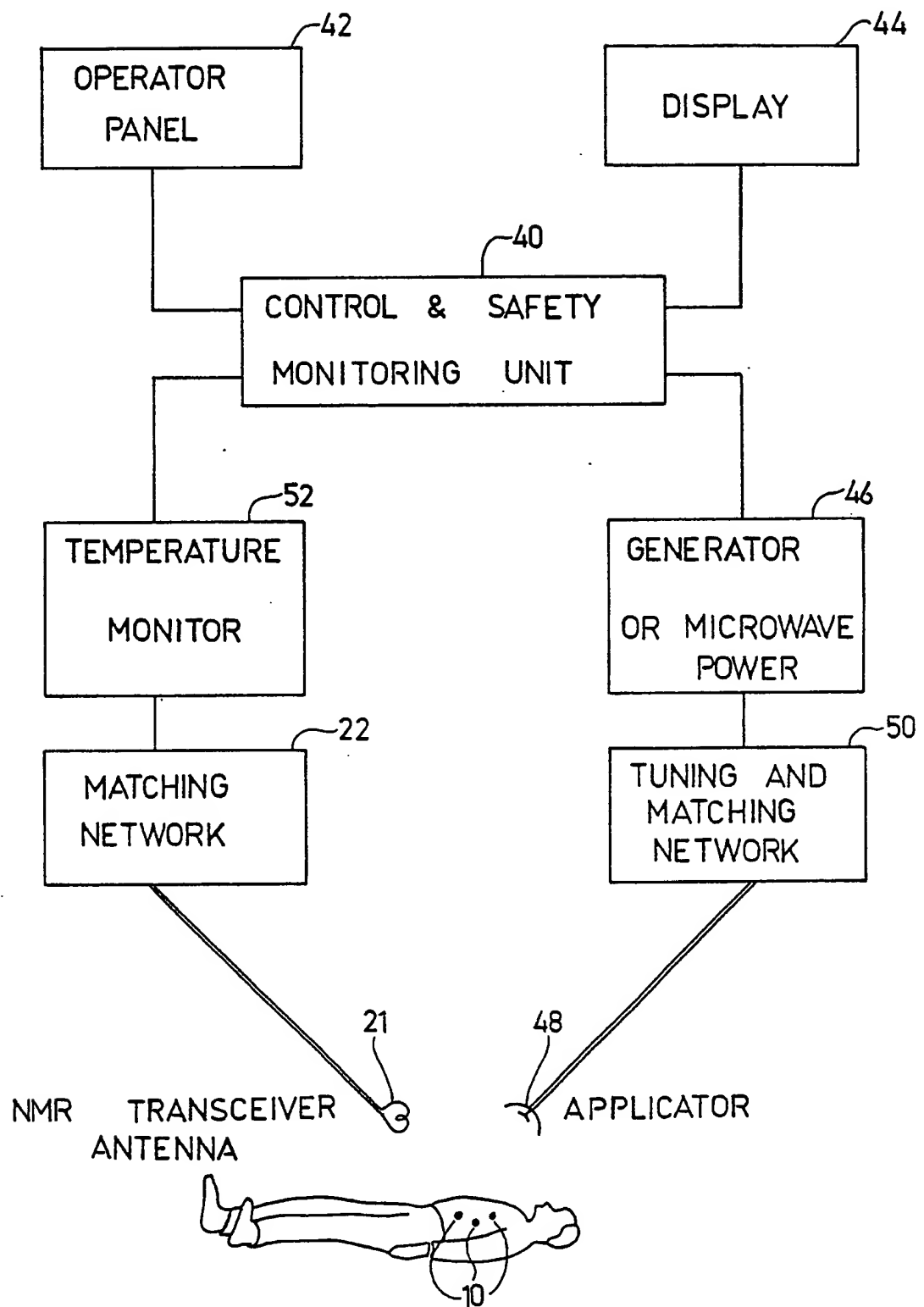
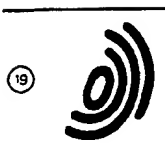


FIG. 1

FIG. 2





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(71) Applicant: **Taicher, Zvi**  
**25 Ben Yehuda Street**  
**Rehovot(IL)**

(72) Inventor: **Taicher, Zvi**  
**25 Ben Yehuda Street**  
**Rehovot(IL)**  
Inventor: **Shporer, Mordechai**  
**14 Shachar Street**  
**Rehovot(IL)**

(74) Representative: **JENSEN & SON**  
**8 Fulwood Place High Holborn**  
**London WC1V 6HG(GB)**

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DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)		
X	EP-A-0 095 124 (BRUKER) * Page 5, lines 15-26; page 11, lines 1-32 * - - -	1,3,6	G 01 N 24/08 G 01 K 1/02 G 01 K 13/00		
A A,D	JOURNAL OF THE PHYSICAL SOCIETY OF JAPAN, vol. 17, no. 4, April 1962, pages 654-659; S. OGAWA et al.: "Nuclear magnetic resonance of Fe57 in various ferrimagnetic oxides" * Chapter: "Introduction" * - - -	4,7 2			
Y	EP-A-0 099 237 (PICKER INT.) * Page 5, line 8 - page 6, line 19 * - - -	8,13			
A	MEDICAL PHYSICS, vol. 10, no. 3, May/June 1983, pages 321-325, Am. Assoc. Phys. Med., New York, US; D.L. PARKER et al.: "Temperature distribution measurements in two-dimensional NMR imaging" * Page 324, left-hand column, line 12 - right-hand column, line 2 * - - -	8,13			
A	11TH EUROPEAN MICROWAVE CONFERENCE, Amsterdam, 7th - 11th September 1981, pages 433-437; F.K. BECKMANN et al.: "Remote temperature sensing in organic tissue by ferrimagnetic resonance frequency measurements" * Chapter: "Principles of the FMR temperature sensing" * - - - - -	1,6	TECHNICAL FIELDS SEARCHED (Int. Cl.5)  G 01 N 24/00		
The present search report has been drawn up for all claims					
Place of search  The Hague		Date of completion of search  30 November 90	Examiner  DIOT P.M.L.		
<table border="0"><tr><td><b>CATEGORY OF CITED DOCUMENTS</b> X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention</td><td>E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons ----- &amp;: member of the same patent family, corresponding document</td></tr></table>				<b>CATEGORY OF CITED DOCUMENTS</b> X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention	E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons ----- &: member of the same patent family, corresponding document
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**14 Shachar Street**  
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